Application No.: 09/427,657 Attorney Docket No: 28967/35061A

IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A method of treating a mammalian subject to inhibit restenosis of a blood vessel, comprising the step of:

administering to a mammalian subject in need of treatment to inhibit restenosis of a blood vessel a composition comprising a replication-deficient adenovirus comprising a polynucleotide,

wherein said composition is administered locally at the site in need of treatment to inhibit restenosis,

wherein said polynucleotide comprises a nucleotide sequence that encodes a vascular endothelial growth factor C (VEGF-C) polypeptide operatively linked to a promoter to promote expression of the VEGF-C polypeptide in cells of the blood vessel,

wherein the VEGF-C polypeptide comprises ~~an amino acid sequence selected from the group consisting of:~~

~~(a)~~ the amino acid sequence of SEQ ID NO: 2;

~~(b) analogs of (a) in which from 1 to 21 amino acids have been added, deleted, or replaced with other amino acids, wherein the analogs bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3; and~~

~~(c) fragments of (a) or (b), wherein the fragments bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3,~~ and

wherein expression of said VEGF-C polypeptide in said blood vessel cells inhibits restenosis of said blood vessel.

2. (original) A method according to claim 1 wherein said mammalian subject is human.

3-9. (canceled)

10. (previously presented) A method according to claim 1 wherein the polynucleotide further comprises a polyadenylation sequence operably connected to the sequence that encodes the VEGF-C polypeptide.

11. (original) A method according to claim 2 wherein the composition further comprises a pharmaceutically acceptable carrier.

12-13. (canceled)

14. (previously presented) A method according to claim 2 wherein said administering comprises at least one intravascular injection of said composition.

15. (previously presented) A method according to claim 2 wherein said administering comprises a catheter-mediated transfer of said composition into a blood vessel of the mammalian subject.

16. (original) A method according to claim 15 wherein said catheter-mediated gene transfer comprises introducing a catheter into a coronary artery of the mammalian subject, and releasing the composition into the coronary artery.

17. (original) A method according to claim 2 wherein said administering is conducted in said human concurrently with a percutaneous transluminal coronary angioplasty.

18. (currently amended) A treatment to inhibit restenosis of a blood vessel in a human, comprising delivering a replication-deficient adenovirus vector to the vessel, said vector comprising a polynucleotide encoding a VEGF-C polypeptide, and further comprising a promoter sequence to promote expression of the VEGF-C polypeptide in cells of the blood vessel, wherein expression of said VEGF-C polypeptide in said blood vessel cells inhibits restenosis of the blood vessel, and

wherein the VEGF-C polypeptide comprises ~~an amino acid sequence selected from the group consisting of:~~

~~(a)~~ the amino acid sequence of SEQ ID NO: 2. ~~2;~~

~~(b) analogs of (a) in which from 1 to 21 amino acids have been added, deleted, or replaced with other amino acids, wherein the analogs bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3; and~~

~~(c) fragments of (a) or (b), wherein the fragments bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3.~~

19-21. (canceled)

22. (currently amended) An improvement in a medical device designed to contact a surface of a blood vessel in the course of surgery to treat stenosis of the blood vessel, said improvement comprising integrating into the device a composition effective to prevent restenosis, said composition comprising a replication-deficient adenovirus comprising a VEGF-C polynucleotide operatively linked to a promoter that promotes expression of a VEGF-C polypeptide encoded by the polynucleotide in cells of blood vessels,

wherein the VEGF-C polypeptide comprises ~~an amino acid sequence selected from the group consisting of:~~

~~(a)~~ the amino acid sequence of SEQ ID NO: 2. ~~2;~~

~~(b) analogs of (a) in which from 1 to 21 amino acids have been added, deleted, or replaced with other amino acids, wherein the analogs bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3; and~~

~~(c) fragments of (a) or (b), wherein the fragments bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3.~~

23. (original) The improvement of claim 22, wherein the device is selected from the group consisting of intravascular stents, intravascular catheters, and combinations thereof.

24. (original) The improvement of claim 22, wherein the device comprises an extravascular collar.

25. (original) The improvement of claim 22, wherein the device comprises an elastomeric membrane adapted to cover a surface of an intravascular stent or catheter.

26. (currently amended) A medical device comprising an endovascular stent having an outer surface for contacting a surface of a blood vessel, and a composition on said surface, said composition comprising a replication-deficient adenovirus comprising a VEGF-C polynucleotide operatively linked to a promoter that promotes expression of VEGF-C polypeptide encoded by the polynucleotide in cells of blood vessels,

wherein the VEGF-C polypeptide comprises ~~an amino acid sequence selected from the group consisting of:~~

~~(a)~~ the amino acid sequence of SEQ ID NO: 2. ~~2;~~

~~(b) analogs of (a) in which from 1 to 21 amino acids have been added, deleted, or replaced with other amino acids, wherein the analogs bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3; and~~

~~(c) fragments of (a) or (b), wherein the fragments bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3.~~

27. (currently amended) A medical device comprising a catheter having an outer surface for contacting a surface of a blood vessel, and a composition on said surface, said composition comprising a replication-deficient adenovirus comprising a VEGF-C polynucleotide operatively linked to a promoter that promotes expression of VEGF-C polypeptide encoded by the polynucleotide in cells of blood vessels,

wherein the VEGF-C polypeptide comprises ~~an amino acid sequence selected from the group consisting of:~~

~~(a)~~ the amino acid sequence of SEQ ID NO: 2. ~~2;~~

~~(b) analogs of (a) in which from 1 to 21 amino acids have been added, deleted, or replaced with other amino acids, wherein the analogs bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3; and~~

~~(c) fragments of (a) or (b), wherein the fragments bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3.~~

28. (currently amended) A medical device comprising a balloon catheter having a void for holding a therapeutic agent for delivery to the interior of a blood vessel, and a composition contained in the void, the composition comprising a replication-deficient adenovirus comprising a VEGF-C polynucleotide operatively linked to a promoter that promotes expression of VEGF-C polypeptide encoded by the polynucleotide in cells of blood vessels,

wherein the VEGF-C polypeptide comprises ~~an amino acid sequence selected from the group consisting of:~~

~~(a)~~ the amino acid sequence of SEQ ID NO: 2. ~~2;~~

~~(b) analogs of (a) in which from 1 to 21 amino acids have been added, deleted, or replaced with other amino acids, wherein the analogs bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3; and~~

~~(c) fragments of (a) or (b), wherein the fragments bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3.~~

29-48. (canceled).

49. (currently amended) A method of treating a mammalian subject to inhibit restenosis of a blood vessel, comprising:

identifying a mammalian subject that has been or will be treated for a stenosed blood vessel; and

administering to the mammalian subject at the site of the stenosed blood vessel a composition comprising a replication-deficient adenovirus comprising a polynucleotide, said polynucleotide comprising a nucleotide sequence that encodes a vascular endothelial growth factor C (VEGF-C) polypeptide,

wherein the VEGF-C polypeptide comprises ~~an amino acid sequence selected from the group consisting of:~~

~~(a)~~ the amino acid sequence of SEQ ID NO: 2;

~~(b) analogs of (a) in which from 1 to 21 amino acids have been added, deleted, or replaced with other amino acids, wherein the analogs bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3; and~~

~~(c) fragments of (a) or (b), wherein the fragments bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3,~~

wherein the polynucleotide includes a promoter sequence operably linked to the encoding sequence to promote expression of the polypeptide in cells of the blood vessel, and

wherein expression of the VEGF-C polypeptide inhibits restenosis of said blood vessel.

50. (previously presented) A method according to claim 49 wherein said mammalian subject is human.

51. (previously presented) A method according to claim 49 wherein the blood vessel is a coronary artery, and the administering is performed concurrently with percutaneous transluminal coronary angioplasty to treat the stenosed blood vessel.

52-64. (canceled)

65. (previously presented) A method according to claim 49 wherein the composition further comprises a pharmaceutically acceptable carrier.

66. (previously presented) A method according to claim 49 wherein said administering comprises at least one intravascular injection of said composition at the site of the stenosed blood vessel.

67. (previously presented) A method according to claim 49 wherein said administering comprises a catheter-mediated transfer of said composition to the site of the stenosed blood vessel.

68. (previously presented) A method according to claim 49 wherein said catheter-mediated gene transfer comprises introducing a catheter into a coronary artery of the mammalian subject, and releasing the composition into the coronary artery.

69. (previously presented) A method according to claim 49 wherein said administering comprises implanting an intravascular stent in said mammalian subject at the site of the stenosed blood vessel, and wherein the stent is coated or impregnated with the composition.

70. (currently amended) An extravascular collar designed to contact a surface of a blood vessel in the course of surgery to treat stenosis of the blood vessel, the collar comprising an outer wall shaped to surround the outer surface of a blood vessel, wherein the wall encloses a space containing a composition comprising a replication-deficient adenovirus comprising a polynucleotide that comprises a nucleotide sequence encoding a VEGF-C polypeptide,

wherein the VEGF-C polypeptide comprises ~~an amino acid sequence selected from the group consisting of:~~

~~(a)~~ the amino acid sequence of SEQ ID NO: 2;

~~(b) analogs of (a) in which from 1 to 21 amino acids have been added, deleted, or replaced with other amino acids, wherein the analogs bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3; and~~

~~(c) fragments of (a) or (b), wherein the fragments bind to and stimulate phosphorylation of VEGFR-2 or VEGFR-3,~~ and

wherein the polynucleotide further comprises a promoter to promote expression of the polypeptide in mammalian cells.

71-72. (canceled)

73. (currently amended) A method according to any one of claims 2, ~~4, 12,~~ 17, and 50, ~~50, and 53,~~ further comprising administering to said subject an inhibitor of smooth muscle cell growth or migration.

74. (previously presented) A device according to any one of claims claim 22, 26, 27, and 28, wherein the composition further comprises an inhibitor of smooth muscle cell growth or migration.

75-100. (canceled)